

a<sup>3</sup>  
cont changed to alanine (SEQ ID NO:5); and combinations of these mutations. --

**REMARKS**

Claims 1-23 are pending in the application.

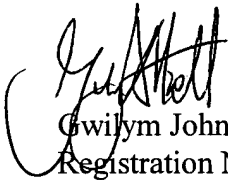
No new matter has been added.

A Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures dated October 23, 2001 has been sent by the Patent Office. In the Notice, Applicant was requested to provide a paper copy of the Sequence Listing as well as a copy of the Sequence Listing in Computer Readable Form correcting certain informalities.

Applicant provides herewith sheets to insert the paper copy of the Sequence Listing. Applicant also provides a copy of the Sequence Listing in Computer Readable Form. Support for the Sequence Listing can be found *inter alia*, on pages 5-6 and Figure 3 of the application as originally filed. In addition, Applicant provides required statements associated with the submission of paper and computer readable copies of Sequence Listings. No new matter has been added.

Claims 1-23 are in condition for allowance. Applicant respectfully requests that this amendment be entered and that claims 1-23 be allowed at this time.

Respectfully submitted,

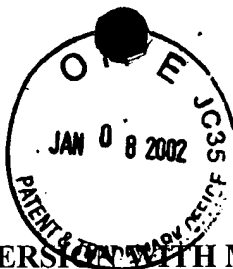
  
Gwilym John Owen Attwell  
Registration No. 45,449

Date: November 20, 2001

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Attachments:      Paper copy of Sequence Listing (pages 1-5)  
                         Sequence Listing in Computer Readable Form  
                         Statement in Support of Sequence Listing  
                         Copy of Notice to Comply  
                         Version With Markings To Show Changes Made

PHOE-0057



VERSION WITH MARKINGS TO SHOW CHANGES MADE

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Please amend the specification as follows:

On page 5, please delete the paragraph beginning with "Figure 3" and insert therefor:

-- Figure 3 is the sequence of secreted (mature) mouse (SEQ ID NO:1) and human (SEQ ID NO:2) TNF. Position 1 is the N-terminus of the secreted TNF. --

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On pages 5-6, please delete the paragraph beginning with "Tumor necrosis factor" and insert therefor:

-- "Tumor necrosis factor" or "TNF" as used herein encompasses either naturally derived protein, such as isolated human or mouse TNF proteins, or protein produced using recombinant technology, such as recombinant murine TNF and recombinant human TNF or various TNF mutant proteins. Although the TNF- $\alpha$  protein is preferred, the term "TNF" also encompasses TNF- $\beta$  protein. The terms also encompass TNF proteins that have been mutated by deletion or alteration of amino acids without significantly impairing biological activity. As non-limiting examples, such mutations include (reference being made to the sequence of the secreted protein, as illustrated in Figure 3): the protein in which amino acids 1-9 (MSTESMIRD (SEQ ID NO:3)) of the human secreted protein are deleted; the protein in which lysine at position 166 is changed to alanine (SEQ ID NO:4), the protein in which lysine at positions 188 and 204 is changed to alanine (SEQ ID NO:5); and combinations of these mutations. --